

Patent Claims:

1. A modified hirudin molecule being substantially non-immunogenic or less immunogenic than non-modified wild-type hirudin having essentially the same biological specificity and activity when used in vivo, comprising amino acid residues substitutions compared with the non-modified parental molecule, which cause a reduction or an elimination of one or more of T-cell epitopes acting in the parental non-modified molecule as MHC class II binding ligands and stimulating T-cells, said modified hirudin molecule has the (M):

V V Y T D C T E S G Q N X¹ C X² C E G S V X³ C G Q G N K C X⁴ X⁵ G S D G E K N Q C X⁶ T G E G
T P X⁷ X⁸ E S H N X⁹ G D X¹⁰ E E I P E E Y L Q

wherein;

X¹ = T or L

X² = T or A or H or Q or T or L;

X³ = A or G or H or K or N or P or Q or R or V;

X⁴ = A or D or E or G or H or K or N or Q or R or S or T or I;

X⁵ = A or D or E or G or H or K or N or P or Q or R or S or T or L;

X⁶ = A or T or V;

X⁷ = T or K;

X⁸ = A or T or P;

X⁹ = E or N or R or D;

X¹⁰ = H or F

and whereby the wild-type sequence (X¹ = L, X² = L, X³ = V, X⁴ = I, X⁵ = L, X⁶ = V, X⁷ = K, X⁸ = P, X⁹ = D and X¹⁰ = F) is excluded.

2. A modified hirudin molecule according to claim 1, wherein

X¹ = L,

X² = L,

X³ = V,

X⁴ = A or D or E or G or H or K or N or Q or R or S or T or I;

X⁵ = A or D or E or G or H or K or N or P or Q or R or S or T or L;

X⁶ = A or T or V;

X⁷ = T or K;

X⁸ = A or T or P;

X⁹ = E or N or R or D; and

X¹⁰ = H or F.

3. A modified hirudin molecule according to claim 2, wherein

$X^6 = V$;

$X^7 = K$;

$X^8 = P$;

5 $X^9 = D$; and

$X^{10} = F$.

4. A modified hirudin molecule according to claim 3, wherein

$X4 = A$ or R , and

10 $X5 = A$ or H .

5. A modified hirudin molecule according to claim 4 having the sequence M1 of Table A.

6. A modified hirudin molecule according to claim 4 having the sequence M2 of Table A.

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7. A modified hirudin molecule according to claim 1 having a sequence selected from the group consisting of M1 – M 81 as specified in Table A.

8. A pharmaceutical composition comprising a modified hirudin molecule of any of the
20 claims 1 – 7, optionally together with a pharmaceutically acceptable carrier diluent or excipient.

9. A peptide molecule having the sequence

CILGSDGEKNQCVTGEGTPKPESHNDGDFE (A)

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or a sequence track consisting of at least 9 consecutive amino acid residues of any of said peptide molecules having a potential MHC class II binding activity and created from the primary sequence of non-modified hirudin, whereby said peptide molecule or sequence track has a stimulation index of > 1.8 in a biological assay of cellular proliferation and said index is taken as the value of cellular proliferation scored following stimulation by a
30 peptide and divided by the value of cellular proliferation scored in control cells not in receipt peptide.

10. Use of a peptide molecule according to claim 8 for the manufacture of a modified hirudin molecule having a modified immunogenicity in a patient.